REMARKS

Applicants respectfully request reconsideration of the Examiner's refusal to recognize priority based on an application filed in Russia on August 18, 2003. Applicants have previously filed and been granted a petition for revival of PCT/EP 2004/009218. Applicants' submit herewith a certified copy of the Russian Priority application no. 2003125486, filed on August 18, 2003, together with an English translation thereof and Declaration of the Translator. Applicants' priority based on the Russian application filed on August 18, 2003, was reinstated. It follows that the Rykova, et al, reference cited by the Examiner to support her rejection of the Claims under 35 U.S.C. 102(a) is moot since the priority date is in 2004, well after applicants' August 18, 2003 priority date.

The Examiner rejected Claims 5-6 and 14 based on Gocke et al, in view of Hefeneider, et al, under 35 U.S.C. 103(a). Applicants respectfully traverse this rejection of their Claims 5-6 and 14.

With respect to Claims 5 and 6, Gocke, et al, describes the isolation of a cell having a mutated oncogene by digesting an amplified nucleic acid fraction with an enzyme that specifically cleaves nucleic acid fragments in the fraction within the nucleotide sequences of nucleic acid fragments.

Gocke et al. does not disclose applicants' step of isolating extracellular nucleic acids bonded to the surface of cells of a cellular fraction and determining by PCR, multiplex PCR, hybridization or sequencing, whether at least two nucleic acids are present among the isolated extracellular nucleic acids. The Examiner admits that Gocke, et al, does not teach wherein the isolation of cell-surface based extracellular nucleic acids comprises the use of PBS/EDTA and a Trypsin treatment as required in Claim 14.

Hefeneider, et al, (2002/0107372) describes extracellular DNA's as being associated with Cystic Firbosis. DNA cells are treated to remove exogenous cell-surface bound nucleic acid. In addition, Hefeneider states that DNA on A549 cells is inhibited by treatment with Trypsin. Further, Hefeneider distinguishes surface binding DNA from internalized plasmid DNA by treating cells with Trypsin to remove cell-surface proteins. Taking Gocke, et al, and Hefeneider, et al, and considering them as a whole they teach the separation of a nucleic acid fraction and treating cells with Trypsin to remove cell-surface proteins. In contrast, applicants' method isolates extracellular nucleic acids and determining by means of PCR, Multiplex, PCR, hybridization or sequencing, whether at least two nucleic acids are present and determining that these nucleic acids are indicative of a disease, such as lung cancer. In addition,

applicants' Claim 14 requires treating cells with 10 volumes of PBS with 5 mmol/1EDTA at 4°C, and after centrifugation, treating the cells with 0.259 Trypsin solution and then inactivating Trypsin with a Trypsin inhibitor, centrifugation, and isolating the extracellular nucleic acids from the collected supernatant. These steps in detail are not found in a combination of Gocke, et al and Hefeneider, et al. It follows that these references fail to make applicants' method of claims 5-6 and 14 obvious within the meaning of 35 U.S.C. 103(a). Therefore this rejection should be withdrawn.

The Examiner's rejected Claim 7 under 35 U.S.C. 103(a) as being unpatentable over Gocke, et al, Hefeneider, et al, and further in view of Zochbauer-Muller. This rejection is respectfully traversed. Gocke, et al, and Hefeneider have been discussed above. Zochbauer-Muller admittedly discloses methylated RASSF - 1A as a diagnostic marker, but discloses it in conjunction with other aberrant methylation markers. Taking the three references together and considering then as a whole, they identify APC and RASSF1A as diagnostic markers for cancers, but in contrast to applicants' method of Claim 7, they do not teach applicants' method of determining the existence of these markers. For this reason, the rejection of Claim 7 under 35 U.S.C. 103(a) should be withdrawn.

In view of all the above, it is believed that Claims 5-7 and 14 are in condition for allowance. Such action is earnestly solicited.

Respectfully submitted,

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Date: 8/25/08

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